petrolatum by heating it to 60° C. Mix with vigorous and continuous agitation. Let cool to room temperature. Continue agitating to effect even dispersion of the hydrocortisone until solidified. The final concentration of CsA is, preferably, 25 mg/ml. The final concentration of hydrocortisone is, preferably, 10 mg/ml.

This formulation is a novel, topical oleaginous, hydrophobic/lipophilic ointment base comprising the combined active ingredients of cyclosporin and a steroid—for example, hydrocortisone. Our results demonstrate that two classes of potent anti-inflammatory agents, cyclosporins and steroids, can successfully be combined in a topical formulation to potentially enhance efficacy. This topical formulation was proven to be efficacious in producing a site-specific localized anti-inflammatory effect and significantly enhanced graft survival compared to matched vehicle-treated controls.

The formulation is advantageous for topical and dermal application due to the chemical properties and hydrophilic/lipophilic balance of the liquid Sandimmune vehicle. The liquid pharmaceutical composition preferably comprises CsA and a carrier consisting of the following: (1) an esterification product (e.g. Labrafil) of natural triglycerides and polyethylene glycol which may be prepared according to U.S. Pat. No. 3,288,824; (2) a vegetable oil; and (3) ethanol.

With heating, and due to the carrier vehicle's chemical properties, hydrocortisone can be partially solubilized independent of prior solubilization in ethanol. Therefore, the solubility of hydrocortisone in ethanol, miscibility of ethanol in the Sandimmune vehicle, and partial hydrocortisone solubility in the vehicle alone serves to facilitate the combination of the two active ingredients in a single topical formulation.

Examples of other steroidal agents that could analogously be combined with cyclosporin(s) in a single topical formulation in order to potentially enhance efficacy include, but are not limited to, the following: betamethasone dipropionate; betamethasone valerate; fluocinolone acetonide; triamcinolone acetonide; prednisone; methylprednisolone; and prednisolone.

b. Anti-Inflammatory Agents and Cyclosporin

Examples of non-steroidal anti-inflammatory agents that could analogously be combined with cyclosporins in a single topical formulation in order to potentially enhance efficacy include, but are not limited to: indomethacin; sulindac; ibuprofen; aspirin; naproxen; and tolmetin.

c. Immunosuppressive Agents and Cyclosporin

Examples of immunosuppressive agents that could analogously be combined with cyclosporin(s) in a single topical formulation in order to potentially enhance efficacy include, but are not limited to, the following: azathioprine; cyclophosphamide; the macrolide FK-506; deoxyspergualin; bredinin; didemnin B; methotrexate; and thalidomide.

What is claimed is:

1. A method for treating T-cell mediated immune processes, allograft rejection, inflammations, autoimmune conditions or cyclosporin-responsive conditions in animals, comprising: topically applying a formulation containing cyclosporin in pharmaceutically effective amounts to the affected tissue; and systemically administering a formulation containing cyclosporin in pharmaceutically effective amounts in conjunction with said topical application.

2. A method according to claim 1, further comprising: initiating said systemic administration prior to said administration of topical cyclosporin, and discontinuing said systemic administration prior to discontinuing said topical administration.

3. A method according to claim 1, further comprising: initiating said systemic administration at a first dosage level prior to initiating said topical administration, and lowering said systemic dosage to a second level during said topical administration.

4. A method according to claim 2 or 3, wherein the topically-applied formulation comprises from about 0.2% to 25% cyclosporin by weight, and is applied to the tissue in such an amount that from about 0.5 mg/cm^2 to 5 mg/cm^2 of cyclosporin is applied per single dose, and further, wherein the systemically-applied cyclosporin-containing formulation is applied in such an amount that from about 1 mg/kg/day to 15 mg/kg/day of cyclosporin is applied per single dosage.

5. A method according to claim 4, wherein the topically-applied formulation contains from about 0.5% to 15% cyclosporin, by weight.

6. A method according to claim 5, wherein the topically-applied formulation containing cyclosporin further comprises one or more of the following:

a pharmaceutical carrier;

a co-solvent;

a penetration enhancer; and

an emulsifier.

7. A method according to claim 6, wherein the pharmaceutical carrier is a solvent, diluent, or carrier selected from the group consisting of waxes, cellulose derivatives, mineral oils, vegetable oils, petroleum derivatives, water, methylcellulose or paraffin, beeswax, glyceryl stearate, PEG-2 stearate, propylene glycol stearate, glycol stearate, cetyl alcohol, steryl alcohol and other similar agents, anhydrous lanolin, white petrolatum, liquid petrolatum, olive oil, ethanol, ethanol-polysorbate 80 solutions, propylene glycol-water solutions, and jojoba oils, and any mixture thereof.

8. A method according to claim 6, wherein the co-solvent is selected from the group consisting of ethanol; oleyl alcohol; alkylene polyols; glycerol; polyethylene glycol; oleic acids; vegetable oil PEG-6 complexes; caprylrc triglyceride; capric triglyceride; glyceryl caprylate; glyceryl caprate; PEG-8 caprylate; PEG-8 caprate; ethoxydiglycol; and any mixture thereof.

9. A method according to claim 6, wherein the penetration enhancer is selected from the group consisting of ethanol; oleyl alcohol; alkylene polyols; oleic acids; urea; pyrrolidones; surfactants; vegetable oil PEG-6 complexes; caprylic triglyceride; capric trrglyceride; glyceryl caprylate; glyceryl caprate; PEG-8 caprylate; PEG-8 caprate; ethoxydiglycol; and any mixture thereof.

10. A method according to claim 6, wherein the emulsifier is selected from a group consisting of PEG stearate and glycol stearate, PEG-6-32-stearate; PEG-6 stearate; polysorbate 80, sodium lauryl sulfate, potassium methyl sulfate, potassium butyl sulfate, sodium tetrapropylene benzene sulfonate, dodecyl trimethyl ammonium chloride, lauric diethanolamide, cetrimide, cetomacrogol, and any mixture thereof.

11. A method according to claim 6, wherein the topical formulation is an ointment.

12. A method according to claim 6, wherein the topical formulation is a paste.